

## SUPPLEMENTARY DATA

# **Cognitive Impairment and Metabolite Profile Alterations in the Hippocampus and Cortex of Male and Female Mice Exposed to a Fat and Sugar-Rich Diet are Normalized by Diet Reversal**

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**Supplementary table 1.** ANOVA P-values for metabolite concentrations in the hippocampus and cortex during 1 to 16 weeks of HFHSD exposure.

<b>Metabolite</b>	<b>Brain area</b>	<b>Interaction</b>	<b>Time</b>	<b>Diet</b>
Alanine	hippocampus	<b>P=0.008</b>	<b>P&lt;0.001</b>	P=0.371
	<b>cortex</b>	<b>P&lt;0.001</b>	<b>P&lt;0.001</b>	<b>P&lt;0.001</b>
Aspartate	hippocampus	P=0.501	P=0.764	P=0.256
	cortex	P=0.394	P=0.703	P=0.572
Creatine	hippocampus	P=0.061	<b>P&lt;0.001</b>	<b>P&lt;0.001</b>
	cortex	P=0.747	<b>P=0.029</b>	P=0.431
Phosphocreatine	hippocampus	P<0.001	<b>P=0.016</b>	P=0.005
	cortex	P=0.743	<b>P&lt;0.001</b>	P=0.857
GABA	hippocampus	<b>P=0.003</b>	P=0.200	P=0.199
	cortex	P=0.528	<b>P=0.047</b>	P=0.880
Glutamine	hippocampus	P=0.390	<b>P=0.023</b>	<b>P=0.018</b>
	cortex	P=0.313	<b>P=0.002</b>	<b>P&lt;0.001</b>
Glutamate	hippocampus	<b>P&lt;0.001</b>	<b>P=0.029</b>	<b>P&lt;0.001</b>
	cortex	P=0.072	<b>P&lt;0.001</b>	P=0.421
Glutathione	hippocampus	<b>P=0.016</b>	P=0.398	P=0.296
	cortex	P=0.184	<b>P&lt;0.001</b>	<b>P=0.015</b>
Glycine	hippocampus	P=0.243	P=0.481	P=0.624
	cortex	P=0.542	<b>P&lt;0.001</b>	<b>P=0.002</b>
<i>myo</i> -inositol	hippocampus	<b>P=0.026</b>	P=0.063	P=0.242
	cortex	P=0.750	<b>P&lt;0.001</b>	P=0.528
Lactate	hippocampus	<b>P&lt;0.001</b>	<b>P&lt;0.001</b>	<b>P&lt;0.001</b>
	cortex	P=0.367	<b>P=0.002</b>	P=0.329
NAA	hippocampus	<b>P&lt;0.001</b>	<b>P&lt;0.001</b>	<b>P&lt;0.001</b>
	cortex	<b>P=0.033</b>	<b>P=0.034</b>	P=0.113
Taurine	hippocampus	<b>P&lt;0.001</b>	<b>P&lt;0.001</b>	<b>P&lt;0.001</b>
	cortex	P=0.989	<b>P&lt;0.001</b>	P=0.281
Ascorbate	hippocampus	P=0.084	<b>P=0.001</b>	P=0.888
	cortex	P=0.989	<b>P&lt;0.001</b>	P=0.281
Glucose	hippocampus	P=0.484	<b>P&lt;0.001</b>	P=0.069
	cortex	P=0.680	<b>P=0.001</b>	<b>P=0.011</b>
NAAG	hippocampus	<b>P=0.042</b>	P=0.364	P=0.151
	cortex	P=0.424	P=0.573	P=0.351
PE	hippocampus	P=0.716	P=0.138	P=0.229
	cortex	P=0.602	<b>P=0.042</b>	P=0.474
Total choline	hippocampus	<b>P=0.042</b>	<b>P=0.042</b>	<b>P=0.042</b>
	cortex	P=0.165	<b>P=0.042</b>	P=0.632
Total creatine	hippocampus	<b>P=0.042</b>	<b>P=0.042</b>	<b>P=0.042</b>
	cortex	P=0.661	<b>P=0.042</b>	P=0.768
PCr/Cr	hippocampus	<b>P=0.042</b>	P=0.274	P=0.932
	cortex	P=0.836	<b>P=0.042</b>	P=0.560

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**Supplementary table 2.** ANOVA P-values for metabolite concentrations in the hippocampus and cortex at 24 weeks of the study.

<b>Metabolite</b>	<b>Brain area</b>	<b>ANOVA at 24 weeks</b>
Alanine	hippocampus	P=0.966
	cortex	<b>P=0.042</b>
Aspartate	hippocampus	P=0.343
	cortex	P=0.580
Creatine (Cr)	hippocampus	P=0.776
	cortex	<b>P=0.042</b>
Phosphocreatine (PCr)	hippocampus	<b>P=0.042</b>
	cortex	P=0.903
GABA	hippocampus	<b>P=0.042</b>
	cortex	P=0.781
Glutamine	hippocampus	P=0.150
	cortex	<b>P=0.042</b>
Glutamate	hippocampus	P<0.001
	cortex	P=0.069
Glutathione	hippocampus	<b>P=0.042</b>
	cortex	<b>P=0.042</b>
Glycine	hippocampus	P=0.205
	cortex	<b>P=0.042</b>
<i>myo</i> -inositol	hippocampus	<b>P=0.042</b>
	cortex	P=0.138
Lactate	hippocampus	<b>P=0.042</b>
	cortex	P=0.058
NAA	hippocampus	P=0.064
	cortex	<b>P=0.042</b>
Taurine	hippocampus	<b>P=0.042</b>
	cortex	P=0.542
Ascorbate	hippocampus	P=0.433
	cortex	P=0.533
Glucose	hippocampus	P=0.490
	cortex	P=0.644
NAAG	hippocampus	P=0.819
	cortex	P=0.061
PE	hippocampus	<b>P=0.042</b>
	cortex	P=0.938
Total choline	hippocampus	P=0.063
	cortex	P=0.326
Total creatine	hippocampus	<b>P=0.042</b>
	cortex	P=0.154
PCr/Cr	hippocampus	P=0.122
	cortex	<b>P=0.042</b>